REMARKS

Claims 1-6, 8-19, 21-32, 34, 35, 37, 47, 50, 57, 60, 62-78, 80, 83, 85 and 87 are pending in this application. Claim 16 is amended. Claims 1-6, 8-15, 17-18, 25, 26, 28, 47, 57, 62-63, 66-78, 80, 83, 85 and 87 were previously withdrawn. Claims 16, 19, 21-24, 27, 29-32, 34-35, 37, 50, 60, and 64-65 are under currently examination. Claims 1-6, 8-19, 21-32, 34, 35, 37, 47, 50, 57, 60, 62-78, 80, 83, 85 and 87 will be pending in this application upon entry of this amendment.

Reference is made to the published application, US 2006/0140984, unless otherwise noted.

Claim 16 is amended to recite that the composition is an oil-in-water emulsion, and to limit the foam adjuvant to fatty alcohols having 15 or more carbons in their carbon chain, fatty acids having 16 or more carbons in their carbon chain, and hydroxy-substituted fatty acids. These amendments are supported by the specification (*see, e.g.*, ¶¶ 25, 56, 81, 82), therefore, no new matter is added.

Rejection Under 35 U.S.C. § 103(a)

Claims 16, 19, 21-24, 27, 29-32, 34, 35, 37, 50, 60 and 64-65 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. 6,730,288 ("Abram") in view of U.S. 6,299,900 ("Reed") and U.S. 2002/0182162 ("Shahinpoor").

Independent claim 16 is set forth in the listing of claims. Claims 19, 21-24, 27, 29-32, 34, 35, 37, 50, 60 and 64-65 depend directly or indirectly from claim 16, and therefore include all of the limitations of claim 16.

The instant claims are directed to a pharmaceutical composition including an active agent, compressed gas propellant, and a foamable carrier including about 2-75 wt% ***petrolatum-free***, ***liquid***, non-volatile hydrophobic solvent; about 25-98 wt% water; about 0.1 wt% to 5 wt% foam adjuvant; about 0.1 wt% to 5 wt% surface-active agent; and about 0.1 wt% to 5 wt% by weight of composition water gelling agent (all percentages by weight of composition), wherein the composition forms an oil-in-water emulsion when placed in a container and combined with the

propellant. The instant claims are also directed to a thermally stable breakable foam that collapses upon application of sheer force.

The previous Office Action dated September 14, 2010, asserted that Abram discloses all the elements of the claimed invention, except using an active agent – for which it relied on Reed and Shahinpoor. The previous Office Action asserted that Abram discloses a "liquid, non-volatile hydrophobic solvent," relying on disclosure of several "[s]uitable occlusive agents" at col. 2, lines 42-45 that include mineral oils.

The present Office Action relies on these assertions and maintains the same rejection (Office Action at page 3, first paragraph).

Applicants previously explained that Abram does not teach compositions without petrolatum or compositions that contain a gelling agent. See response dated December 14, 2009. Applications repeat and maintain those arguments.

The present Office Action states that these arguments are "unpersuasive, because ABRAM teaches using other occlusive agents, such as mineral oil, and is not limited by the examples. Thus it would have been obvious to one skilled in the art to use petrolatum ***or*** mineral oil" (Office Action at page 4, first paragraph, emphasis added). Thus the crux of the instant § 103 rejection is the proposition that mineral oil and petrolatum are interchangeable materials.

Applicants respectfully disagree. Abram discloses an occlusive formulation (Abram at col. 1, lines 60-65). One of ordinary skill in the art would not substitute mineral oil for petrolatum in an occlusive formulation because these two materials are not interchangeable in such formulations.

First, mineral oil and petrolatum are not interchangeable for use as an occlusive agent:

> Mineral oil has sometimes been characterized as providing some occlusivity, which is related to skin moisturization. But this assertion is not supported by data from transepidermal water loss measurements, which provide a fairly direct indication of occlusivity.

> A recent study shows that "***the major ingredient affecting occlusivity of the O/W emulsion systems is petrolatum, not mineral oil***." (Emphasis added).

DiSapio, "Silicones as Alternatives to Hydrocarbons in Personal Care Formulations," Dow Corning U.S.A. 1993, at page 3, col. 1, last paragraph (attached as Exhibit A).[1]

In support, Disapio cites Wang et al., *J. Soc. Cos. Chem.* 39:137-157 (1988) (attached as Exhibit B). Wang prepared 36 different formulations using different amounts of petrolatum, oil, and water. The combination of petrolatum, mineral oil, and water always totaled 78.9% of the 36 test formulations. Wang at page 141, "Formulation Design," and at page 142, Table 2. Wang tested the transepidermal water loss (TWEL) of these formulations on the wrist and forearm of human volunteers using an evaporimeter. Wang at page 143, "Transepidermal Water Loss Determination (TWEL)." Wang concludes that:

> Increasing the amount of mineral oil from 0% to 10% at a constant percentage of petrolatum did not materially affect the TEWL value. On the other hand, increasing the concentration of petrolatum at a constant level of mineral oil decreased the TEWL values.

Wang at page 150. Wang also concludes that "This study shows that petrolatum, ***not mineral oil***, is the key ingredient providing the occlusivity of the o/w emulsion system" (Wang at 155, emphasis added).

Abram also used the TEWL test to assess the occlusivity of the foam formulation (Abram at col. 6, lines 19-60; Figures 2-4). Abram states:

> FIG. 2 clearly shows the relationship between the % of petrolatum content in each of the test mousses and the resultant relative change in the rate of TEWL determined at 30 and 120 minutes after formulation application.
>
> ....
>
> Increasing the concentration of petrolatum in topical mousse formulations was able to decrease the normal rate of TEWL on the

[1] Available at http://www.dowcorning.com.cn/zh_CN/content/publishedlit/25-528-93.pdf.

> forearm of a healthy volunteer. The decreases in the rate TEWL observed effectively demonstrate that increasing the concentration of petrolatum in the product leads to an increase in the relative occlusivity of the topical mousse formulations tested.

Abram at col. 6, lines 48-60. Therefore, Abram, like Wang, teaches that petrolatum is an occlusive agent, and that increasing the amount of petrolatum in a formulation will increase the formulation's occlusivity. Abram provides no teaching contrary to Wang to indicate that mineral oil, by itself, may be used as an occlusive agent.

The cited art teaches at most that mineral oil may be used ***with*** petrolatum, but not that mineral oil may be used ***instead of*** petrolatum. Whenever Abram mentions using mineral oil, Abram requires the concurrent use of greases (Abram at col. 2, lines 42-44; claims 3 and 21). Greases are highly viscous semi-solids, including petrolatum. Thus Abram requires the concurrent use of a viscous occlusive agent with mineral oil. Consistent with this teaching, all of Abram's examples include petrolatum (Abram at Table 1) and Abram states that petrolatum is a preferred occlusive agent (Abram at col. 2, lines 45-46). Shahinpoor discloses only one formulation, and it includes ***both*** mineral oil and petrolatum (Shahinpoor at ¶ 13). None of the Office Actions issued in this application explain why one of ordinary skill in the art would use mineral oil alone without petrolatum, based on the cited art. Furthermore, the Office Action provides no rationale to explain why one of ordinary skill in the art would ignore Abram's disclosure of petrolatum as a preferred occlusive agent, and instead use mineral oil to make a foam.

Thus one of ordinary skill at the time of the invention would appreciate that petrolatum is an occlusive agent, and that mineral oil is not. Therefore, one of ordinary skill in the art would not replace petrolatum with mineral oil in Abram's occlusive formulation.

Furthermore, foamable emulsions based on liquid oils such as mineral oils are much more complicated and challenging to stabilize than petrolatum-based emulsions. One of ordinary skill in the art would appreciate the difficulties associated with forming foams from mineral oil, as compared to petrolatum, and therefore would not be motivated to replace petrolatum with mineral oil in Abram's occlusive formulation.

As an example of the challenge in preparing foamable compositions based on liquid oils such as mineral oils, petrolatum and mineral oil have different stabilization requirements for use in foamable emulsion compositions. Emulsions are inherently thermodynamically unstable systems. In the case of oil-in-water emulsions, coalescence occurs when oil droplets merge together to form larger oil droplets, resulting in phase separation. As the dispersed phase viscosity increases, the coalescence efficiency invariable decreases, leading to stable emulsions. Conversely, lower dispersed phase viscosity leads to unstable emulsions. Thus, foamable emulsions made with liquid oils, where the viscosity of the dispersed phase is low (as is the case with liquid oils like mineral oil), will have a much higher inherent instability than foamable emulsions made with petrolatum where the viscosity of the dispersed phase is higher.

The tendency of emulsion oil droplets to coalesce and the consequent susceptibility of emulsion to break down with lower viscosity of the oil in the emulsion, is demonstrated by Hu et al., *Physics of Fluids* 12(3):484-489 (2000) (attached as Exhibit C)[2] and Kumar et al., *Chemical Engineering Science* 48:2025–2038 (1993) (attached as Exhibit D)[3].

Finally, petrolatum is a semi-solid unctuous material with high viscosity, whereas mineral oil is a liquid oil with low viscosity. Thus they are physically different materials.

Applicants have surprisingly discovered that foams formed from emulsions of liquid oils can be stabilized using the claimed foam adjuvants in combination with a water gelling agent. None of the cited art teaches or suggests Applicants' solution to this problem.

In summary,

[2] Hu studied the influence viscosity and examined the ratio between the viscosity of the internal phase and the viscosity of the continuous phase ("ratio λ"); and their data showed that the ratio λ (is inversely correlated with droplet coalescence rate, that is as the ratio increases the coalescence is lower. So foamable emulsions made with liquid oils, where the viscosity ratio λ is low, will have a much higher inherent instability than foamable emulsions made with petrolatum where the viscosity ratio λ is higher.

[3] Kumar also confirmed the dependence of the droplet coalescence on dispersed phase viscosity. Their data show that as the dispersed phase viscosity increases, the coalescence efficiency invariable decreases and that low dispersed phase viscosity leads to unstable emulsions.

(1) Abram does not teach or suggest the substitution of petrolatum for mineral oil in an occlusive foam composition because mineral oil, absent petrolatum, is not occlusive.

(2) One would not be motivated to substitute mineral oil for petrolatum in *any* formulation because it is is more difficult to formulate stable foam compositions using liquid oils.

(3) Abram does not teach or suggest the recited foam adjuvants that can improve the foaming capacity of surfactants and/or to stabilize the foam made from compositions using liquid oils.

(4) Abram does not teach or suggest a water gelling agent.

(5) Petrolatum and mineral oil are physically different materials and not substitutable.

Applicants submit that for at least these reasons, mineral oil and petrolatum are not interchangeable materials for use in occlusive formulations. Therefore, one of ordinary skill in the art would not use mineral oil alone without petrolatum in the formulations disclosed by the cited references. Thus the cited references do not render the instant claims obvious.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 16, 19, 21-24, 27, 29-32, 34, 35, 37, 50, 60 and 64-65 under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above amendment and remarks, Applicants believe that the pending application is in condition for allowance.

A Request for Continued Examination and a request for a three month extension of time are filed with this response. Please charge the required fees to our Deposit Account No. 08-0219, under Order No. 0113873.124US2 from which the undersigned is authorized to draw. Applicant believes no other fee is due with this response. However, if another fee is due, please charge our Deposit Account No. 08-0219, under Order No. 0113873.00124US2 from which the undersigned is authorized to draw.

Respectfully submitted,

Dated: September 3, 2010

/Andrew Zoltan/
Andrew Zoltan
Registration No.: 64,929
Attorney for Applicant(s)

Wilmer Cutler Pickering Hale and Dorr LLP
399 Park Avenue
New York, NY 10022
(212) 230-8800 (telephone)
(212) 230-8888 (facsimile)